Unipolar Depression Management Protocol

All Team Members: Patient Self-Management Education & Support

Unipolar depression or Major Depressive Disorder means that the patient feels persistent low mood or inability to enjoy activities that are usually enjoyable nearly every day for two weeks. It is associated with a higher risk of suicide, substance abuse, and chronic pain.

Sleep hygiene	Patient should use their bed for sleep and sex only. Move the television out of the bedroom. Develop a regular and relaxing routine for bedtime. Set a regular time to get up and get dressed each day. Drink caffeinated beverages in the morning only.
Exercise	Exercise is an excellent antidepressant. This exercise need not be strenuous. Daily walking for 30 minutes is enough. Do some exercise outside the house every day, if possible. Aerobic exercise (walking, swimming, running, biking) is best but strength building (weight lifting and using exercise machines) also helps.
Social activation	People with depression tend to isolate themselves and constantly think about their failings. It is important that they remain connected with family and friends, even if they do not feel like it. They should schedule meetings and activities that they used to enjoy. This is adopting the "fake it until you make it approach."
Quit drugs. Limit alcohol	Many illicit drugs, like cocaine and methamphetamines, elevate mood in the short-term, but make depression worse over time. Alcohol will reduce anxiety in the short-term, but worsens depression and increases risk of suicide. Alcohol makes falling asleep easier, but

	staying asleep harder. Support your patients to quit.
Take medications as directed	Patient will usually be prescribed: - Antidepressant - Possibly another medicine (lithium, pramipexole…) Many patients also take dietary supplements, alternative medications (such as SAMe) or herbal medications. Ask about these to see if there are interactions with prescribed drugs or toxic side effects. Talk to the patients to see if they are taking their prescribed medicines and if there are barriers to adherence.

Educate the patient about warning signs of worsening depression or risk of suicide and when to call the team:

- Persistent thoughts of killing themselves, especially with a specific plan
- Access to weapons or other dangerous means of hurting themselves
- Substance abuse or increased use
- Increasing anxiety
- Increasing social isolation: not spending time with other people
- Increasing anhedonia: not enjoying the things/activities they used to enjoy
- Increasing feelings of hopelessness
- Increasing difficulty with sleep
- Difficulty doing the basic activities of daily life (food preparation, paying bills, keeping themselves clean)

NP

1. Standard Depression Care:

Initial visit	**Every month**
A. Assess depressive symptoms (PHQ-9) B. Confirm diagnosis, rule out manic/hypomanic episodes, review past episodes of depression and treatments received	Assess depressive symptoms (PHQ-9)
C. Assess anxiety symptoms (GAD-7, panic screen)	Assess anxiety symptoms (GAD-7)
D. Screen for PTSD (PC-PTSD)	
E. Assess for alcohol	

abuse and drug abuse F. Medication reconciliation and management	
G. Review self-management plan and barriers to / achievement of goals • Review use of alcohol, tobacco, illicit drugs and alternative therapies • Review activity diary documenting behavioral and social activation • Review any hopelessness and suicidal ideation	

A. Assess depression symptoms with PHQ-9:
    1. English version: http://www.depression-primarycare.org/images/pdf/phq_9_eng.pdf
    2. Spanish version: http://www.depression-primarycare.org/images/pdf/phq_9_spanish.pdf
    ii. Score 0-4: within normal range,
    iii. Score 5-9: sub-clinical depressive symptoms,
    iv. Score 10-14: likely mild depressive disorder,
    v. Score 15-27: likely moderate to severe depressive disorder

B.

C. Confirm unipolar depression diagnosis
    i. Confirm Major depressive episode (MDE).
        1. Minimum duration: 2 weeks
        2. At least 5 symptoms required
            a. At least one of first two*:
                i. decreased mood*
                ii. anhedonia*
                iii. insomnia or hypersomnia
                iv. guilt/worthlessness
                v. lack of energy
                vi. impaired concentration/focus/thinking
                vii. significant weight loss or weight gain (unintentional) from appetite change
                viii. psychomotor slowing or acceleration

ix. recurrent thoughts of death / suicidal ideation

ii. Rule out manic episode (antidepressant monotherapy not indicated if patient has history of mania or hypomania—see bipolar protocol).
    1. Minimum duration: 1 week (this is crucial to avoid overdiagnosis of bipolar disorder)
        a. functionally impairing symptoms which include:
            i. Elevated mood (plus 3 additional symptoms)
            ii. Irritable mood (plus 4 additional symptoms)
            iii. Additional symptoms:
                1. distractibility
                2. decreased need for sleep (most helpful)
                3. grandiosity
                4. flight of ideas
                5. increased goal-directed activity (e.g., a flurry of plans to start new businesses, ventures, or exotic travel—often with poor follow-through)
                6. increased pleasure-seeking (e.g., sexual or financial disinhibition or indiscretions)
                7. pressured speech
        b. NOT occurring in the context of drug or medication use (esp. stimulants)
    2. Rule out Hypomanic episode
        a. Minimum duration: 4 days (crucial)
        b. By definition, NOT functionally impairing.
        c. NOT occurring in the context of drug abuse (esp. stimulants)
        d. Otherwise similar to manic episode above
    3. Dysthymic disorder
        a. 2 years of subsyndromal depression (i.e. does not meet criteria for Major Depressive Disorder) without hypomania
        b. May occur with Major Depression ("double depression")
        c. Requires 2 of the following:
            i. Sleep disturbance
            ii. Appetite disturbance
            iii. Decreased energy
            iv. Decreased [self-]esteem
            v. Decreased concentration

vi. Hopelessness

D. Consider possible medical causes of mood disorder
    i. Common medical etiologies (not an exhaustive list)
        1. Hypothyroidism (worth screening all patients with TSH), anemia, hypogonadal hypogonadism, Vitamin B-12 deficiency
        2. Neurological disorders: multiple sclerosis, Parkinson's Disease
        3. Collagen-vascular disorders: systemic lupus erythematosis
    ii. Substance etiologies (not an exhaustive list)
        1. Sedative and alcohol abuse
        2. Stimulant withdrawal
        3. Interferon treatment

E. Discuss depression diagnosis with patient, who may be reluctant to accept this diagnosis. Helpful points for discussion include:
    i. Depression is common.
    ii. Depression is associated with both emotional symptoms (mood changes) and physical symptoms (ie, headache, abdominal pain).
    iii. Depression is associated with changes in brain neurochemistry.
    iv. Treatment with medication and/or psychotherapy generally shortens the course of depression and diminishes symptoms.
    v. Unless there is a concern for suicidality, patients who are uncomfortable with a diagnosis of depression can initially be observed with short-term follow-up (eg, two weeks) arranged.

F. Psychotherapy: It is important to talk to your patients about psychotherapy for the treatment of unipolar depression. An enormous body of evidence exists that supports the use of Interpersonal Therapy, Cognitive-Behavioral Therapy, and Behavioral Activation Therapy in the treatment of depression. Studies indicate that psychotherapy and antidepressant therapies work equally well, and either one can be a first choice of therapy for mild to moderate depression. Severe depression warrants choosing a medication as first stage of treatment. Combining psychotherapy and antidepressant medications works better than either one alone.

G. Medication management:

i. Recommend antidepressant treatment, especially for patients with moderate to severe depression (PHQ-9 =15 or more). If patients refuse antidepressant treatment, utilize behavioral activation and problem-solving therapy. Continue to monitor depressive symptoms and recommend antidepressants if PHQ-9 is $\geq$ 15.
ii. Patients treated with medication should be told the following:
    1. Do not stop medications without talking with the prescribing clinician. Call to discuss side effects or other questions
    2. It may take two to three weeks before medications begin to relieve symptoms
    3. Early side effects, such as nervousness, headache and stomach upset may occur, but are often gone after the first 2 weeks
    4. It is important to continue a full course of antidepressant therapy (usually 6 to 12 months), even if symptoms are alleviated in the first month, to prevent early relapse
    5. Sexual side effects are common, especially difficulty achieving an orgasm. Sometimes switching anti-depressants can be helpful, or augmenting with other medications. Patients should be warned about sexual side effects, and encouraged to discuss them if they occur.
iii. Psychotherapy can be an option for patients with mild to moderate major depression. In primary care, depression-specific psychotherapies produce outcomes similar to pharmacotherapy.
iv. The major classes of antidepressants are 1) tricyclic antidepressants [TCAs], 2) monoamine oxidase inhibitors [MAOIs] 3)selective serotonin reuptake inhibitors [SSRIs], 4) inhibitors of the reuptake of both serotonin and norepinephrine [SNRIs], 5) norepinephrine reuptake inhibitors, and 6) some medications with unique modes of action.
v. See table below for available antidepressants

Usual daily dose of antidepressants for adults
[brackets indicates no generic available]

Drug	Starting dose per day (mg)*	Usual total dose per day for treatment of depression (mg)
Selective serotonin reuptake inhibitors		
Citalopram	10 to 20	20 to 40•
Escitalopram	10	10 to 20
Fluoxetine	10 to 20	20 to 60
Fluvoxamine	50	50 to 300Δ
[Fluvoxamine CR	100	100 to 300]
Paroxetine	10 to 20	20 to 60
Paroxetine CR	12.5 to 25	25 to 75
Sertraline	50	50 to 200
Serotonin-norepinephrine reuptake inhibitors		
Venlafaxine	37.5	75 to 300 (as 2-3 divided doses)
Venlafaxine XR	37.5	75 to 300
[Desvenlafaxine	50	50 (no titration)]
[Duloxetine	30	60 to 120Δ]
Dopamine-norepinephrine reuptake inhibitors		
Bupropion	75 to 150 (as 2 divided doses)	300 to 350
Bupropion SR 12 hour	100	300 to 350
Bupropion XL 24 hour	150	300 to 350
Serotonin modulators		
Nefazodone◊	50	300 to 600 (as 2 divided doses)
Trazodone	50	75 to 500Δ
[Trazodone ER	75	75 to 375]
Noradrenergic and specific serotonergic antidepressant		
Mirtazapine	15	15 to 45

Tricyclics and tetracyclics

Amitriptyline	25 to 50	100 to 300$^{\Delta}$
Amoxapine	50	100 to 400$^{\Delta}$
Clomipramine	25	100 to 250$^{\Delta}$
Desipramine	25 to 50	100 to 300$^{\Delta}$
Doxepin	25 to 50	100 to 300$^{\Delta}$
Imipramine	25 to 50	100 to 300$^{\Delta}$
Maprotiline	50	100 to 225$^{\Delta}$
Nortriptyline	25	50 to 150$^{\Delta}$
Protriptyline	10	15 to 60 as three or four divided doses
Trimipramine	25 to 50	100 to 200$^{\Delta}$

Monamine oxidase inhibitors

Isocarboxazid	10	10 to 40 as two to four divided doses
Phenelzine	15	15 to 90 as three or four divided doses
Selegiline transdermal	6 mg patch	6 to 12 patch
Tranylcypromine	10	30 to 60 as three or four divided doses

Total daily dose shown is for oral administration, except as noted.
* A lower starting dose may be necessary in the elderly or in patients with significant comorbidities. Lower initial doses may also reduce the incidence of adverse events, including anxiety, in some patients.
• Maximum recommended dose of citalopram is 20 mg for patients >60 years of age, with significant hepatic insufficiency, or taking interacting medications that can increase citalopram levels. Other patients should not exceed 40mg.
Δ As two or three divided doses or may be given as a single dose at bedtime, except if dose is at upper end of range.
◊ Caution: can cause liver failure. Not available in Europe, Canada, and several other countries.

Medication and class-specific caveats:

1. Sexual side-effects: The most common sexual side-effects are decreased libido and delayed orgasm. Evidence suggests that 50% of patients with this from SSRI treatment will experience an improvement if bupropion is added. Another option is to add sildenafil, even in females.
2. Medication-Medication Interactions: Of all of the SSRIs, Fluoxetine, Fluvoxamine and Paroxetine have the most medication interactions. Nefazodone also has significant medication interactions. Use an interaction checking program.

3. If considering starting a TCA, guidelines suggest checking an ECG in patients over 40 years old to rule out dysrhythmias and prolonged intervals. This class is to be avoided in patients with heart block given the risk of lethal dysrhythmias. Additionally, TCAs are extremely lethal in overdose, and should not be used if a patient is acutely suicidal with intent. Patients must secure these medications at home so that small children or demented adults do not overdose on them.
4. Bupropion at high doses lowers the seizure threshold. As a result, this is not an ideal choice in a patient with epilepsy, history of head injury, or any use of cocaine or methamphetamine.
5. MAOIs require significant dietary restrictions and have significant medication-medication interactions. These should only be started after consultation with the IAP team. They must never be mixed with other monoamine-increasing substances, such as antidepressants or stimulants.
6. Mirtazapine, amitriptyline, and paroxetine can cause significant weight gain. This requires monitoring.

vi. Examples of how some antidepressants can be started

1] Citalopram (most easily tolerated SSRI)

a) start at 20mg qAM after breakfast

b) start at 10mg qAM after breakfast if high anxiety, panic, elderly, or frail; advance to 20mg after first week if tolerating

c) may advance to 40 mg after one month, do not exceed 40mg as higher doses associated with QTc prolongation

d) short-term side effects (usually remit in first week): nausea, diarrhea, headache, jitters, anxiety

e) long-term side effects (will last as long as med is taken): decreased libido

2] bupoprion (activating, non-SSRI)

a) can use once daily XL formulation which is now generic

b) start 150mg qAM with food

c) start 75mg qAM of immediate release if high anxiety, panic, elderly, or frail; advance to 150mg after first week if tolerating

d) maximum dose is 450mg; Recommend keeping dose below 350mg as doses above 400mg increase seizure risk. This is coumponded by any other substance that lowers the seizure threshold. Avoid in cocaine or methamphetamine users for this reason.

e) short-term side effects (usually remit in first week): agitation, jitters, anxiety, dry mouth

f) long-term side effects (will last as long as med is taken): rarely insomnia or agitation, systolic hypertension

3] nortriptyline (most usable tricyclic)

a) useful when pain relief (esp neuropathic) or sleep continuity are important

b) start 25mg qHS, advance by 25mg per 2-4 weeks, may start at 10mg for frail

c) no maximum dose, but rarely need to exceed 150mg

d) can be used in combination with SSRI, though there is small risk of toxic serum drug levels or serotonin syndrome

e) side effects (worst in first week, but may persist): dry mouth, constipation, jitters, dizziness, palpitations

f) use with caution and use lower doses in the elderly

g) do not use this class in anyone with heart block on ECG

4] venlafaxine (only generic SNRI, this class is effective for pain relief)

a) begin 75mg qAM of XR formulation, 37.5 for frail, elderly, anxious

b) may advance by 75mg every 2 to 4 weeks, top FDA approved dose is 225mg, but 300mg often useful and safe

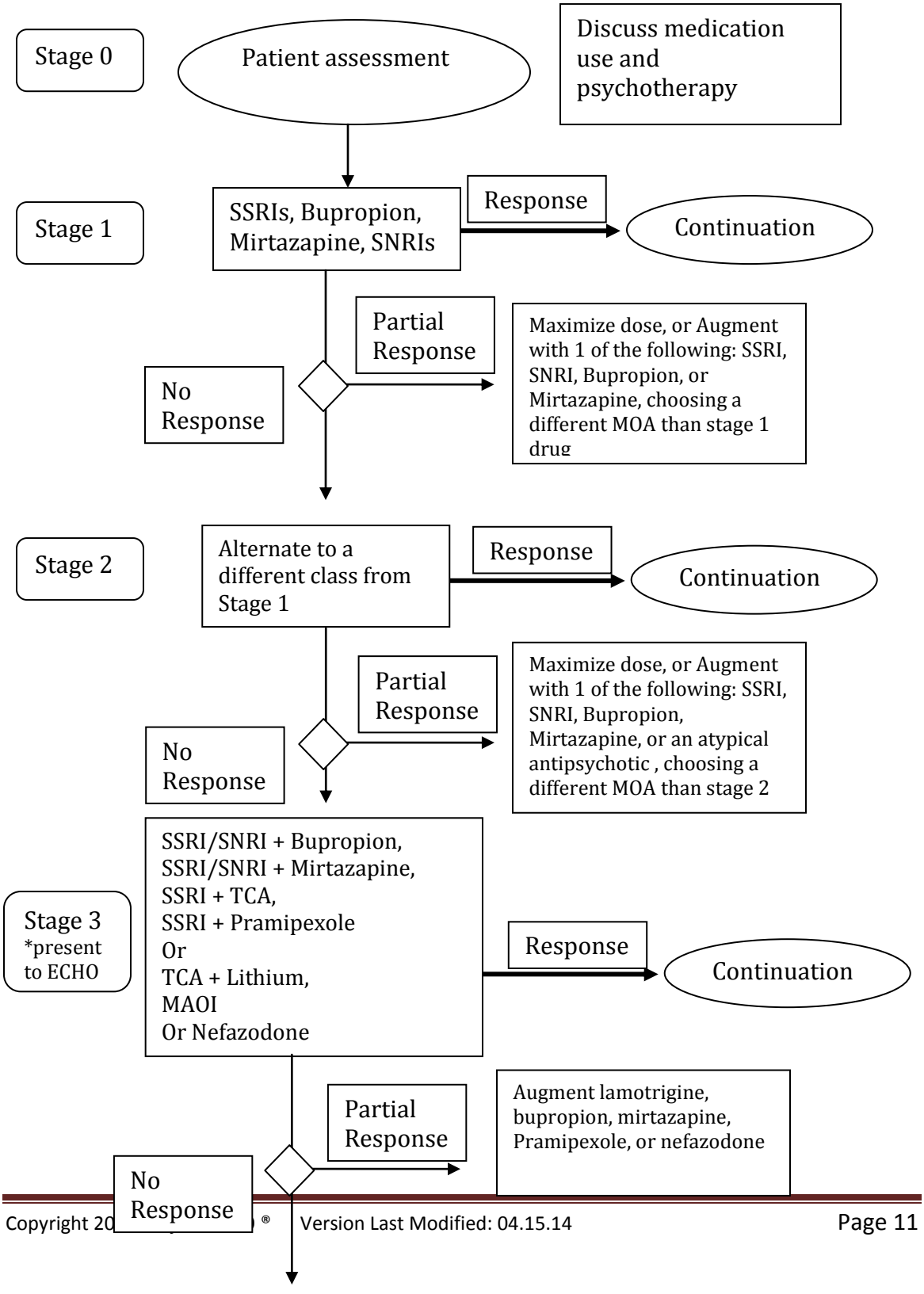
c) short-term side effects (usually remit in first week): agitation, jitters, anxiety, dry mouth

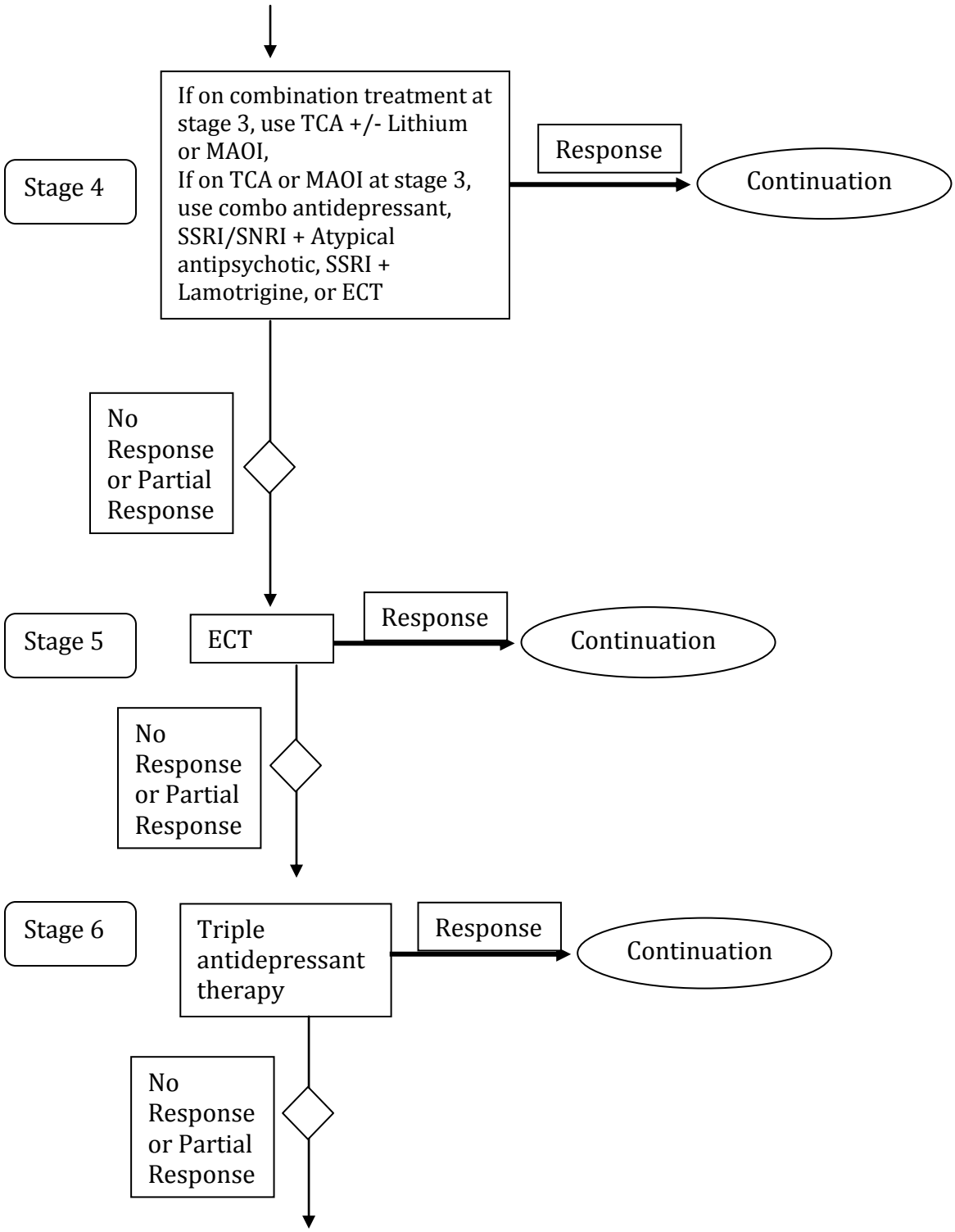
d) long-term side effects (will last as long as med is taken): rarely insomnia or agitation, systolic hypertension

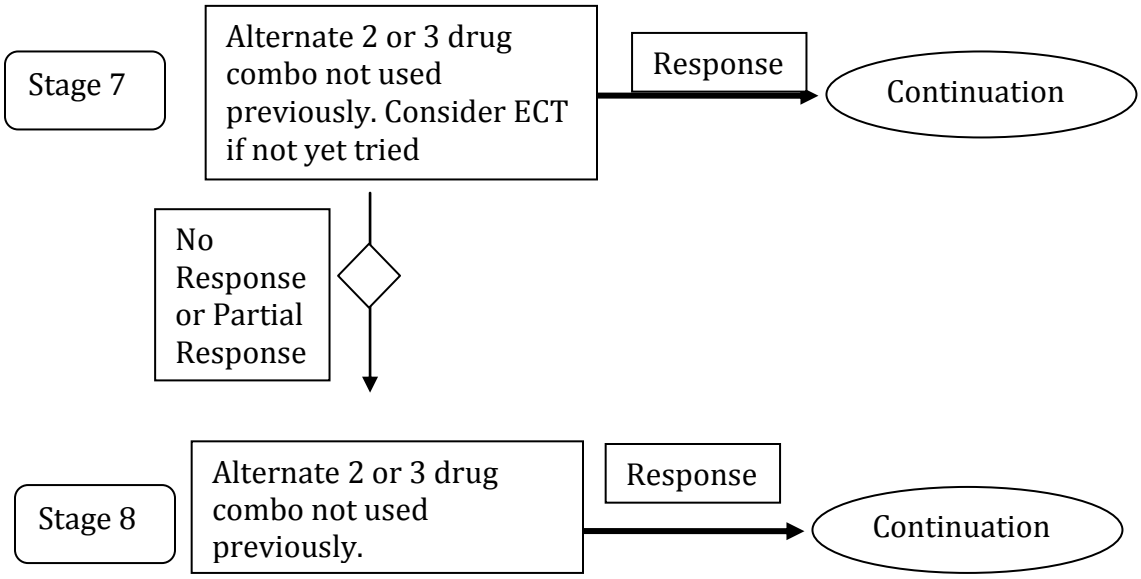
vii. Risks of antidepressant use

a. Suicidal ideation (i.e. suicidality)can be present after initiation of antidepressant treatment. Tell patients to call you right away if they feel more hopeless or suicidal. Adolescents may be at highest risk for exacerbation of suicidal thoughts. Tricyclics can be fatal in overdose.
b. Unopposed antidepressants are not safe in patients with bipolar disorder because they can induce mania. Patients with mood lability that lasts hours rather than days generally do not have bipolar disorder, but a personality disorder, such as borderline personality disorder. Antidepressants are only marginally effective in patients with borderline personality disorder.

MAJOR DEPRESSIVE DISORDER TREATMENT ALGORITHM (adapted from the Texas Medication Algorithm Project)

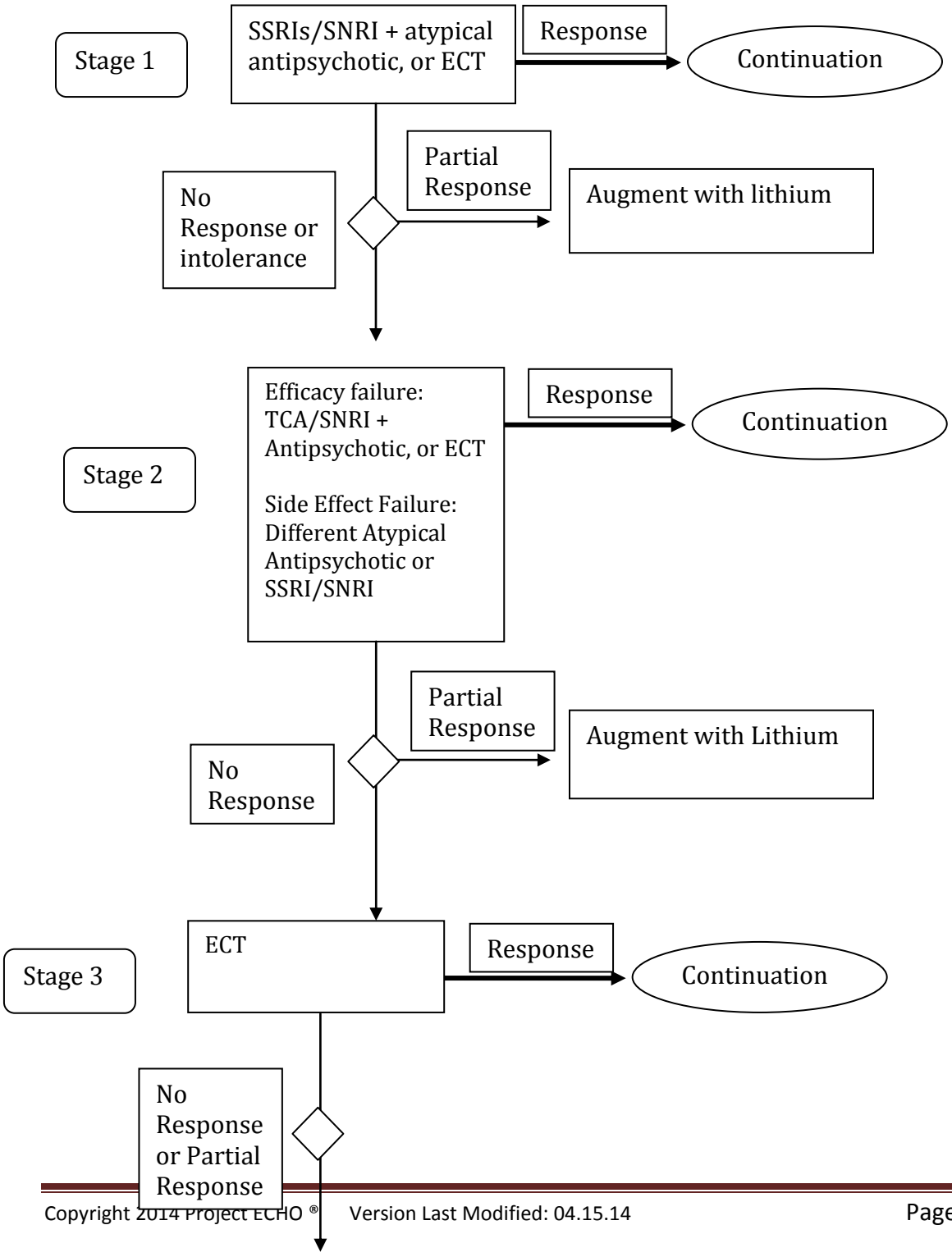


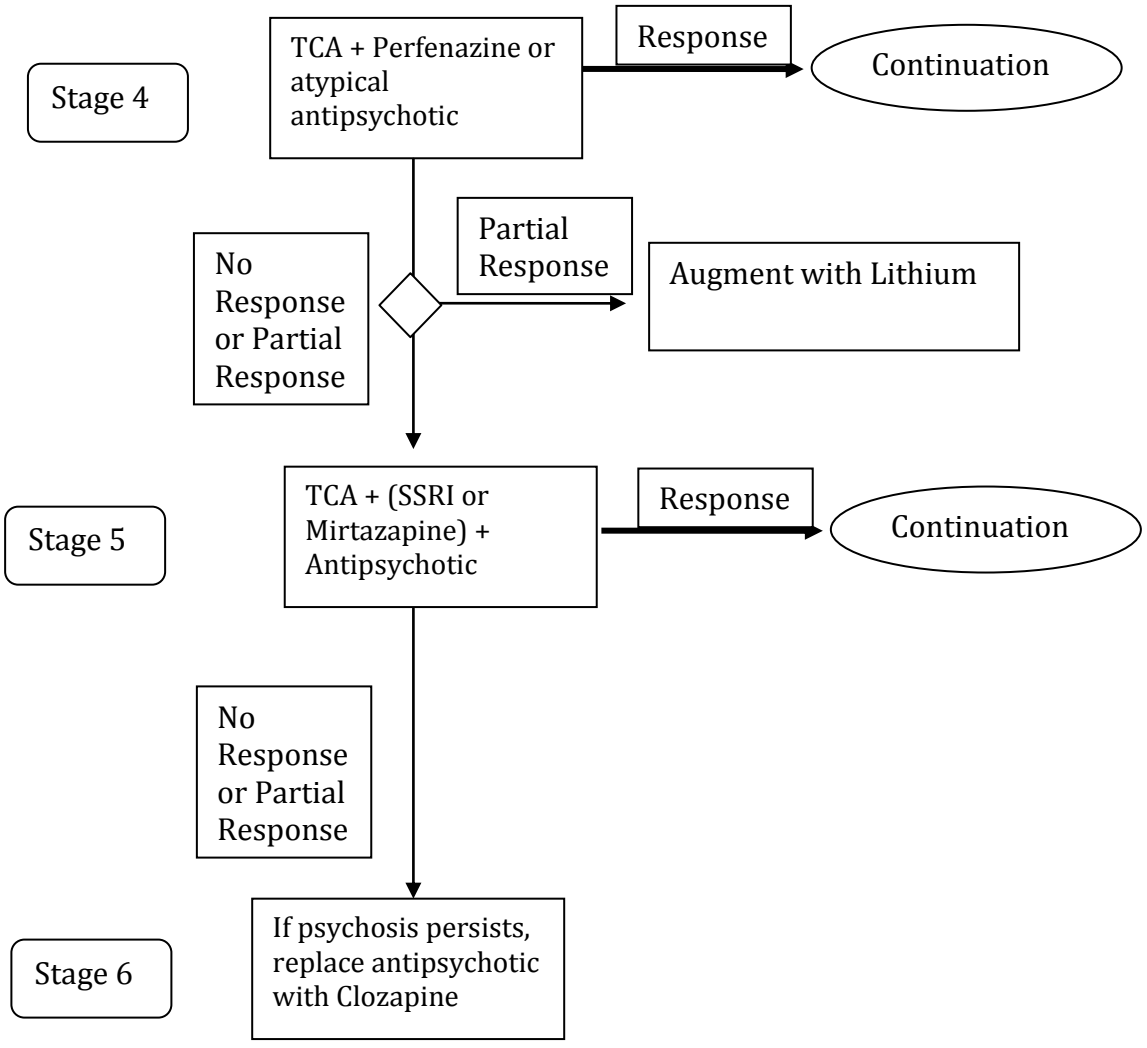

Stage 4
If on combination treatment at stage 3, use TCA +/- Lithium or MAOI,
If on TCA or MAOI at stage 3, use combo antidepressant, SSRI/SNRI + Atypical antipsychotic, SSRI + Lamotrigine, or ECT
Response
Continuation
No Response or Partial Response
Stage 5
ECT
Response
Continuation
No Response or Partial Response
Stage 6
Triple antidepressant therapy
Response
Continuation
No Response or Partial Response



Continuation: 6-9 months of treatment after symptom remission with agent(s) that worked

MAJOR DEPRESSIVE DISORDER <u>WITH PSYCHOTIC FEATURES</u> TREATMENT ALGORITHM (adapted from the Texas Medication Algorithm Project)





Continuation: 4 months of treatment on antipsychotic and lifetime on antidepressant

CHW

A. Review the medication list and assess if there are problems with adherence
B. Review daily activity pattern – is patient confined to house, to bedroom?
C. Reinforce sleep hygiene, scheduling of pleasant activities
D. Review use of alcohol, illicit drugs, sedatives, stimulants Make sure patient is aware of dangers of these and how they interfere with depression treatment
E. Review available social supports and strategies for reducing social isolation, encourage patient to attend church or other social groups in which they have previously participated
F. Review patient self-management goals and action plan
G. Help address financial barriers to reactivation and recovery
H. Explore if any social pathways need to be added, revisited or updated.
    a. Consider referrals to county/state agencies for Medicaid, other funding assistance (likewise for federal agencies—e.g., for SSI, SSDI, Medicare, etc.)
    b. Consider referrals to subsidized housing.
    c. Consider referrals to supported employment.
I. Asses for suicide or harm-
    a. Asses if the patient has plans to harm themselves or others,
    b. Asses of the patient's behavior is so disturbing it is affecting other people
J. Listen Non Judgmentally-
    a. Be empathetic when listening to the patient
    b. Make sure they listen and understand everything that is being said
    c. Make them feel like they won't be judged for speaking freely
    d. Give information and reassurance
    e. Once your patient has been heard they are more likely to accept encouragement
K. Offer reassurance like: emotional support be empathetic about how they may feel or think
L. Encourage the appropriate professional help
M. Inform them that they can access support in a number of ways
N. Their family can even receive support to support them better
O. Talk to them about medications they can take and how to deal with stigma
P. Explore that there is counseling and psychological therapy
Q. Encourage self-help and OTHER SUPPORT STRATEGIES
R. Encourage your patient to seek support from family, friends or support groups in their area.

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